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(FILE 'HOME' ENTERED AT 18:09:28 ON 24 JUN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:09:50 ON 24 JUN 2003

L1 140161 S (TREAT? OR RESCU? OR REPOPULAT?)(8A)(DYSTROPH? OR RETINA OR N
L2 1755 S (NEURAL OR NEURON)(3A)PROGENITOR(W)CELL
L3 140 S L1 AND L2
L4 75 S L1(S)L2
L5 28 S L1(8A)L2
L6 16 DUP REM L5 (12 DUPLICATES REMOVED)
L7 29 S L1(10A)L2
L8 16 DUP REM L6 (0 DUPLICATES REMOVED)
L9 17 DUP REM L7 (12 DUPLICATES REMOVED)

=> d au ti so ab 1-17 l9

L9 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Bertilsson, Goran; Frisen, Jonas; Falk, Anna; Heidrich, Jessica; Hellstrom, Kristina; Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jaccqueline; Mercer, Alex; Patrone, Cesare; Ronnholm, Harriet; Wikstrom, Lilian; Zachrisson, Olof
TI The functional role and potential therapeutic use of Reelin, Gas6 and Protein S in relation to adult neural stem or progenitor cells
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
AB The invention relates generally to methods of influencing central nervous system cells to produce progeny useful in the treatment of CNS disorders. More specifically, the invention includes methods of exposing a patient suffering from such a disorder to reagent that modulates the proliferation, migration, differentiation and survival of central nervous system cells via Reelin, Gas6 or Protein S signaling. These methods are useful for reducing at least one symptom of the disorder.

L9 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Yu, John S.; Kabos, Peter; Ehtesham, Moneeb
TI Differentiation of whole bone marrow
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
AB A method is described for generating a clin. significant vol. of neural progenitor cells from whole bone marrow. A mass of bone marrow cells may be grown in a culture supplemented with fibroblast growth factor-2 (FGF-2) and epidermal growth factor (EGF). Further methods of the present invention are directed to utilizing the **neural progenitor cells** cultured in this fashion in the **treatment** of various **neuropathol**. conditions, and in targeting delivery of cells transfected with a particular gene to diseased or damaged tissue.

L9 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Carpenter, Melissa K.; Denham, Jerrod J.; Inokuma, Margaret S.; Thies, Scott R.
TI Dopaminergic neurons and proliferation-competent precursor cells for treating Parkinson's disease and for use in drug screening
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
AB The invention provides improved methods for obtaining populations of neural progenitor cells and differentiated neurons from pluripotent stem cells. The technol. can be used to produce progenitors that proliferate through at least 40 doublings, while maintaining the ability to differentiate into a variety of different neural phenotypes. Cell populations have been obtained that contain a high proportion of cells staining for tyrosine hydroxylase, which is a feature of dopaminergic

neurons. The neural progenitors and terminally differentiated neurons of the invention can be generated in large quantities for use in drug screening and the treatment of clin. important neurol. disorders, such as Parkinson's disease.

L9 ANSWER 4 OF 17 MEDLINE DUPLICATE 1
AU Nixon Kimberly; Crews Fulton T
TI Binge ethanol exposure decreases neurogenesis in adult rat hippocampus.
SO JOURNAL OF NEUROCHEMISTRY, (2002 Dec) 83 (5) 1087-93.
Journal code: 2985190R. ISSN: 0022-3042.
AB Alcoholism is associated with cognitive deficits and loss of brain mass. Recent studies have indicated that neural progenitor cells proliferate throughout life forming neurons, astrocytes, and oligodendrocytes. The dentate gyrus is one neurogenic region of the adult brain containing neural progenitor cells. To determine if binge ethanol (EtOH) exposure alters neural progenitor cell proliferation and survival, bromodeoxyuridine was administered to adult male rats following an acute or chronic binge exposure paradigm. For an acute binge, rats were gavaged with a 5 g/kg dose of EtOH or vehicle, administered bromodeoxyuridine, and killed either 5 h or 28 days after EtOH treatment. In a 4-day, chronic-binge paradigm, rats were infused with EtOH three times per day (mean dose 9.3 g/kg/day) or isocaloric control diet. Rats were given bromodeoxyuridine once a day for the 4 days of chronic binge treatment, then perfused either immediately following the last dose of EtOH or 28 days later. In both EtOH **treatment** groups, binge EtOH decreased **neural progenitor cell** proliferation.
Following the chronic four-day binge, neural progenitor cell survival was decreased. These studies are the first to show EtOH inhibition of neural progenitor cell proliferation and survival in the adult, a possible new mechanism underlying alcoholic cognitive dysfunction.

L9 ANSWER 5 OF 17 MEDLINE DUPLICATE 2
AU Amano Toshiyuki; Inamura Takanori; Wu Chun-Ming; Kura Shinobu; Nakamizo Akira; Inoha Satoshi; Miyazono Masayuki; Ikezaki Kiyonobu
TI Effects of single low dose irradiation on subventricular zone cells in juvenile rat brain.
SO NEUROLOGICAL RESEARCH, (2002 Dec) 24 (8) 809-16.
Journal code: 7905298. ISSN: 0161-6412.
AB Although the juvenile human brain is relatively radioresistant, irradiation can result in brain growth retardation, progressive mental disturbance, and neurologic abnormalities. As neural stem cells or progenitor cells may be a target of radiation injury and may play an important role in the brain's functional recovery, we examined the effects of whole brain irradiation on these cells in juvenile rat. Six-week-old Wistar rats, where the brain is still growing, were irradiated with single doses of 1, 2, or 3 Gy X-ray. We measured their body and brain weights at 30 or 60 days after irradiation. The chronological changes of the subventricular zone (SVZ) were examined at 6 h, 2, 7, 14, 30, or 60 days after irradiation by immunohistochemistry, specifically looking at the neural stem cells or progenitor cells using anti-nestin antibodies specific for these cells. The rate of brain weight gain of irradiated rats significantly decreased in comparison to controls, although that of body weight gain was similar among them. Multiple apoptotic cells appeared in the SVZ at 6 h after irradiation with simultaneous reduction in nestin-positive cells (69% of the control). The cell levels recovered within a week, with the nestin-positive cells reaching maximal numbers (182%) on Day 14. Nestin-positive cells returned to baseline levels within 30 days (96%) and remained unchanged for the subsequent 60 days. The X-ray dosage did not affect these findings. Our findings revealed that single low dose X-ray administration reversibly affected the levels of neural stem and progenitor cells in the SVZ region. These results suggest that continuous multiple administrations of X-rays in clinical **treatment** may affect irreversible changes on **neural** stem or **progenitor cells**, causing brain growth retardation,

or dysfunction.

L9 ANSWER 6 OF 17 MEDLINE DUPLICATE 3
AU Kabos Peter; Ehtesham Moneeb; Kabosova Andrea; Black Keith L; Yu John S
TI Generation of neural progenitor cells from whole adult bone marrow.
SO EXPERIMENTAL NEUROLOGY, (2002 Dec) 178 (2) 288-93.
Journal code: 0370712. ISSN: 0014-4886.
AB The efficient and large-scale generation of **neural progenitor cells** for **neural** grafting in the **treatment** of **neurological** diseases has been a challenge. Here we describe the isolation and successful propagation of neural progenitor cells from adult rat bone marrow. Unfractionated bone marrow cultured in vitro with epidermal growth factor and basic fibroblast growth factor gave rise to cellular spheres which differentiated into neurons and glia. The cellular spheres expressed nestin, a neural stem cell marker as well as CD90, a marker of hematopoietic stem cells. This methodology addresses the ethical and tissue rejection problems associated with fetal neural stem cells and would circumvent the difficulty associated with generating neural progenitors from the adult brain. We demonstrate that bone marrow may offer a renewable autologous extracranial source of neural progenitor cells.

L9 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Carpenter, Melissa K.
TI Neural progenitor cell populations obtained from culturing stem cells in cocktail of growth conditions
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
AB The invention provides populations of neural progenitor cells, differentiated neurons, glial cells, and astrocytes. The populations are obtained by culturing stem cell populations (such as embryonic stem cells) in a cocktail of growth conditions that initiates differentiation, and establishes the neural progenitor population. The progenitors can be further differentiated in culture into a variety of different neural phenotypes, including dopaminergic neurons. The differentiated cell populations or the neural progenitors can be generated in large quantities for use in drug screening and the treatment of neurol. disorders.

L9 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AU Tanaka, Akira (1); Kamiakito, Tomoko; Hakamata, Yoji; Fujii, Akiko; Kuriki, Ken; Fukayama, Masashi
TI Extensive neuronal localization and neurotrophic function of fibroblast growth factor 8 in the nervous system.
SO Brain Research, (7 September, 2001) Vol. 912, No. 2, pp. 105-115. print.
ISSN: 0006-8993.
AB Fibroblast growth factor (FGF) 8 has been well established to play a critical role in the early development of the central nervous system (CNS). We report here extensive neuronal localization and neurotrophic function of FGF8 in the nervous system. In sections of mouse embryos at E10.5, FGF8 was immunohistochemically found in neurons at the marginal zones of the CNS and in the dorsal root ganglia (DRG). Neuronal localization of FGF8 was marked at later embryonic stages and in adults, involving most of the central and peripheral neurons, including intermuscular enteric neurons, DRGs, and paraaortic sympathetic ganglia. Functionally, FGF8 promoted neurite outgrowth in human neuroblastoma SK-N-MC cells as well as in rat pheochromocytoma PC12 cells, suggesting that FGF8 acts as a neurotrophic factor. FGF8 also supported neuronal survival and differentiation in cultured human **neural progenitor cells**. In a cell growth assay, **treatment** with 50 ng/ml FGF8 on human cultured **neuroblastoma** SK-N-MC and IMR32 cells attenuated the growth of both. In accordance with these in vitro findings, the immunohistochemical analysis on human neurological diseases showed that FGF8 expression is

evident in differentiating histological types of neuroblastoma and ganglioneuroblastoma, and that the levels of FGF8 immunoreactivity in the substantia nigra from Parkinson's disease are significantly lower than those in age-matched controls. Taken together, the present findings strongly suggest that FGF8 acts as a more generalized neurotrophic factor than previously reported.

L9 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU Jarman, R. G. (1); Schaack, J. B.; Freed, C. R. (1)
TI Human neural progenitor cells can differentiate into neurons in the midbrain of embryonic day 15 rats.
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 56. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
AB Neural progenitor cells isolated from various regions of adult and embryonic brain have been reported to differentiate into neurons in vivo and in vitro. In this study we wished to determine if neural progenitor cells isolated from human embryonic mesencephalon 7 to 8 weeks' post conception can differentiate into tyrosine hydroxylase (TH) positive neurons in developing rat brain. **Neural progenitor cells** were expanded as **neurospheres** with bFGF/EGF **treatment**. After 21 days in culture, **neurospheres** were infected with a non-replicating adenovirus expressing GFP. Five days post-infection, GFP expressing neurospheres were placed in contact with the ventricular surface of the ventral midbrain in vitro. These midbrain whole-mount fragments were cultured in DMEM/F12 with 10% FCS. Two GFP expressing neurospheres were placed on the dorsal surface of the interpeduncular nucleus in the tegmental aqueduct medial to the substantia nigra. Nine days post-transplant, the tissue was sectioned and processed immunohistochemically for TH. Numerous GFP expressing cells with neuronal morphology were observed, though far fewer than the number contained in each neurosphere. A small number of GFP and TH-positive co-expressing cells were observed in the area of the substantia nigra. The majority of the GFP expressing cells that were incorporated into the tissue mass remained within the subventricular zone. This study shows that human neural progenitor cells can respond to signals in ED15 rat mesencephalon to differentiate into dopamine neurons.

L9 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Eriksson, Peter; Orwar, Owe
TI A method for introducing nucleic acids into neural stem or progenitor cells via the inherent transport system of the cell
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
AB A method for introducing a substance comprising a nucleic acid into a mammalian neural stem cell or progenitor cell, characterized in that said nucleic acid directly interacts with the cell membrane of said cell or a component within said cell membrane whereby the substance comprising said nucleic acid is taken up by the cell via the inherent transport mechanism of the cell, is disclosed. The advantages of the present invention are: (1) it does not rely on the binding of DNA to any sol. receptors or carriers; (2) It allows for the selective labeling of cells, due to the fact that only cells with the inherent transport system are transfected. Also different applications of said method are disclosed.

L9 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Eriksson, Peter
TI Growth hormone-modulating agents and method for **treatment** of conditions affecting **neural** stem cells or **progenitor cells**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
AB The invention discloses the use of a substance that, on administration,

will lead to increased concns. of growth hormone, e.g. growth hormone, a functionally equiv. analog thereof, or a substance that will increase the release of endogenous growth hormone, for the prodn. of a medicinal product for **treatment** of abnormal conditions affecting **neural** stem cells, **progenitor cells** and/or cells derived from **neural** stem cells or **progenitor cells**, esp. conditions affecting the oligodendroglia, astroglia, and/or neuronal cells. In vitro and in vivo methods are disclosed for inducing lineage detn., propagating and/or inducing or maintaining the genesis of neurons, oligodendrocytes, astroglial cells from progenitor cells, stem cells and/or cells derived from said cells by administering to the cells a substance that increases the concn. of growth hormone. Also disclosed is a method of reducing the genesis of oligodendrocytes, neurons, or astroglial cells from progenitor cells or stem cells, wherein a pharmaceutically effective amt. of a substance that will lead to a decreased concn. of growth hormone or a functionally equiv. analog thereof is administered to the patient.

L9 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Reid, James Steven; Fallon, James H.
TI Methods for treating neurological deficits
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
AB Methods and compns. are provided for treating a patient who has a neurol. deficit. The method can be carried out, for example, by contacting (in vivo or in culture) a neural progenitor cell of the patient's central nervous system (CNS) with a polypeptide that binds the epidermal growth factor (EGF) receptor and directing progeny of the proliferating progenitor cells to migrate en masse to a region of the CNS in which they will reside and function in a manner sufficient to reduce the neurol. deficit. The method may include a further step in which the progeny of the neural precursor cells are contacted with a compd. that stimulates differentiation.

L9 ANSWER 13 OF 17 MEDLINE DUPLICATE 5
AU Alder J; Lee K J; Jessell T M; Hatten M E
TI Generation of cerebellar granule **neurons** in vivo by transplantation of BMP-**treated neural progenitor cells**.
SO NATURE NEUROSCIENCE, (1999 Jun) 2 (6) 535-40.
Journal code: 9809671. ISSN: 1097-6256.
AB Cerebellar granule neurons, the most abundant class of CNS neurons, have a critical role in cerebellar function. Granule neurons are generated at the dorsal border of the mesencephalon and metencephalon, the rhombic lip. In the mouse embryo, rhombic lip cells express a number of granule neuron markers, notably the bHLH transcription factor Math1. Dorsal midline cells adjacent to the rhombic lip express Bmp6, Bmp7 and Gdf7, three genes encoding peptide growth factors of the bone morphogenetic protein (BMP) family. These BMPs induced the expression of granule neuron markers in cultured neural tissue. Moreover, BMP-treated neural cells formed mature granule neurons after transplantation into the early postnatal cerebellum, suggesting that BMPs initiate the program of granule cell specification.

L9 ANSWER 14 OF 17 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AU Shihabuddin L S (Reprint); Palmer T D; Gage F H
TI The search for neural progenitor cells: prospects for the therapy of neurodegenerative disease
SO MOLECULAR MEDICINE TODAY, (NOV 1999) Vol. 5, No. 11, pp. 474-480.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 1357-4310.
AB The etiology of many neurodegenerative diseases has been identified in recent years. Treatment of central nervous system (CNS) disease could focus on one or more steps that lead to cell loss. In the past decade,

cell therapy and/or ex vivo gene therapy have emerged as possible strategies for the **treatment** of **neurodegenerative** diseases. The ability to grow CNS-derived **neural progenitor cells** using growth factors has been extremely useful to study diverse phenomena including lineage choice, commitment and differentiation. By virtue of their biological properties and their presence in the adult CNS, neural progenitors represent good candidates for multiple cell-based therapies for neural diseases. Further identification of the molecules that direct the differentiation of adult neural progenitors may allow their activation in vivo to induce self-repair. This review addresses the nature, distribution and regulation of neural stem cells and the potential for applying these cells to Both structural CNS repair and gene therapy.

L9 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2003 ACS
IN Luskin, Marla B.
TI Neuronal progenitor cells and uses thereof
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
AB The present invention provides an isolated cellular compn. comprising > .apprx.90% mammalian, non tumor-derived, neuronal progenitor cells which express a neuron-specific marker and which can give rise to progeny which can differentiate into neuronal cells. Also provided are methods of treating neuronal disorders utilizing this cellular compn.

L9 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2003 ACS
AU Martinez-Serrano, Alberto; Lundberg, Cecilia; Horellou, Philippe; Fischer, Walter; Bentlage, Claas; Campbell, Kenneth; Mckay, Ronald D. G.; Mallet, Jacques; Bjoerklund, Anders
TI CNS-derived neural progenitor cells for gene transfer of nerve growth factor to the adult rat brain: complete rescue of axotomized cholinergic neurons after transplantation into the septum
SO Journal of Neuroscience (1995), 15(8), 5668-80
CODEN: JNRSDS; ISSN: 0270-6474
AB A CNS-derived conditionally immortalized temp.-sensitive neural progenitor (CINP) cell line was used to generate NGF-secreting cells suitable for intracerebral transplantation. The cells were transduced by repeated retroviral infection, using a vector contg. the mouse NGF cDNA under the control of the LTR promoter. Subcloning at the permissive temp. (33.degree.) identified a highly NGF-secreting clone (NGF-CINP), which contained multiple copies of the transgene and released NGF at a rate of 2 ng/h/105 cells in vitro, both at 33 and 37.degree., which was approx. 1 order of magnitude higher than what was possible to achieve in the heterogeneously infected cell cultures. After transplantation to the brain, the NGF-CINPs differentiated into cells with a predominant glia-like morphol. and migrated for a distance of 1-1.5 mm from the implantation site into the surrounding host tissue, without any signs of overgrowth and tumor formation. Grafts of NGF-CINP cells implanted into the septum of adult rats with complete fimbria-fornix lesion blocked over 90% of the cholinergic cell loss in the medial septum, and grafts placed in the intact striatum induced accumulation of low-affinity NGF receptor pos. fibers around the implantation site. Expression of the NGF transgene in vivo was demonstrated by RT-PCR at 2 wk after grafting. It is concluded that the immortalized neural progenitors have a no. of advantageous properties that make them highly useful exptl. tools for gene transfer to the adult CNS.

L9 ANSWER 17 OF 17 MEDLINE
AU Kaye E M
TI Therapeutic approaches to lysosomal storage diseases.
SO CURRENT OPINION IN PEDIATRICS, (1995 Dec) 7 (6) 650-4. Ref: 47
Journal code: 9000850. ISSN: 1040-8703.
AB Nascent therapies for the lysosomal storage diseases have begun. The replacement enzyme therapy for Gaucher's disease now includes a

recombinant form, and effective dosing schedules are being developed. Bone marrow transplantation appears to be a very successful treatment for nonneuronopathic Gaucher's disease and halts the progression of other lysosomal storage disorders. Following the success of bone marrow transplantation, gene therapy trials using transduced human hematopoietic cells are beginning in Gaucher's disease, which should lead to autologous bone marrow transplantation using genetically engineered cells. Experimental studies hold promise for **neurologic treatment** in the lysosomal storage diseases using transplanted recombinant cells and **neural progenitor cells**

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L9 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 2000:493693 CAPLUS
DN 133:100460
TI A method for introducing nucleic acids into neural stem or progenitor cells via the inherent transport system of the cell
IN Eriksson, Peter; Orwar, Owe
PA A+ Science Invest AB, Swed.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000042202	A1	20000720	WO 2000-SE73	20000114
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PRAI	SE 1999-134	A	19990115		
	WO 2000-SE73	W	20000114		

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 2000:368139 CAPLUS
DN 132:343355
TI Growth hormone-modulating agents and method for **treatment** of conditions affecting **neural** stem cells or **progenitor cells**
IN Eriksson, Peter
PA A+ Science Invest AB, Swed.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
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PI   WO 2000030675       A2    20000602       WO 1999-SE2197   19991125
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PRAI SE 1998-4064        A     19981125
     WO 1999-SE2197      W     19991125

L9   ANSWER 12 OF 17  CAPLUS  COPYRIGHT 2003 ACS
AN   1999:113564  CAPLUS
DN   130:177542
TI   Methods for treating neurological deficits
IN   Reid, James Steven; Fallon, James H.
PA   The Regents of the University of California, USA
SO   PCT Int. Appl., 100 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
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     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
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     WO 1998-US16281     W     19980804
RE.CNT  8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9   ANSWER 15 OF 17  CAPLUS  COPYRIGHT 2003 ACS
AN   1997:181162  CAPLUS
DN   126:168832
TI   Neuronal progenitor cells and uses thereof
IN   Luskin, Marla B.
PA   Emory University, USA
SO   PCT Int. Appl., 46 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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	WO 1996-US11304	W	19960705		
	US 1998-3006	A3	19980105		

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L4	l2 or L3	421	L4
L3	(neural or neuron) near3 precursor adj cell	258	L3
L2	(neural or neuron) near3 progenitor adj cell	232	L2
L1	(treat$ or rescu$ or repopulat$) near9 (dystroph$ or retina or neur$)	18913	L1

END OF SEARCH HISTORY

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